Time-Stretch Quantitative Phase Imaging for Cancer Detection

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Optical microscopy is a critical tool in many fields of research and medicine, and there is a need for techniques that can provide high-speed, label-free detection. Quantitative phase imaging (QPI) is a promising label-free technique for single-cell analysis for medical or biological research, as it acquires the refractive index and thickness of cells in phase images, and thus can provide chemical-specific information related to cellular characteristics, overcoming the drawbacks of conventional bright-field microscopy.[1] By combining QPI with optofluidic time-stretch microscopy, an image acquisition rate of more than 10,000 frames per second can be achieved, which surpasses the speed limits of conventional microscopy and hence makes QPI a viable candidate for high-throughput detection.[2] Moreover, with computer-assisted analysis of cell morphology and other phenotypes, time-stretch QPI provides high-throughput single-cell analysis without the need for chemical labeling, which has great potential for detecting cancer in its early stages, since it substantially improves the effectiveness of treatment while lowering its cost.[3] However, the applications of existing time-stretch QPI techniques are limited because the techniques require wideband photodetectors, and noise easily introduces errors during phase unwrapping.

Here we present a new method for time-stretch QPI microscopy, designed to overcome the drawbacks of existing techniques. Our technique significantly reduces photodetector bandwidth requirements and the influence of noise on phase unwrapping. As shown in **Figure 1** (a), a beat note is generated upon the interference of the light from the sample arm, which carries cellular information, and the light from the reference arm, the relative frequency of which is shifted by AOMs. The beat note is detected by a photodetector, and the signal is then processed in order for the intensity and phase images of a large number of cells to be recovered simultaneously and subsequently analyzed by deep learning algorithms. Using this device, we have acquired intensity and phase images of leukemia cells flowing at speeds up to 10 m/s, as shown in **Figure 1** (b) and (c). The resolution of the image can be further improved by interpolation (**Figure 1** (d)). Because of its high speed and high sensitivity, the technique we developed could be used for the detection of rare circulating tumor cells (CTCs) in blood, for early-stage cancer diagnosis and treatment.

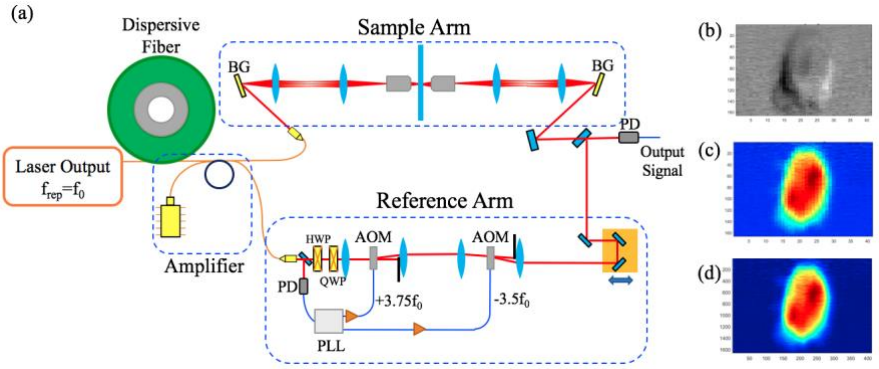

Figure 1: Schematic and experimental results of time-stretch QPI. (a) Optical schematic of device (BG, blazed grating; HWP, Half-wave plate; QWP, Quarter-wave plate; PD, Photodetector; PLL, Phase-locked loop; AOM, Acousto-optic modulator). (b) Recovered intensity image of a K562 cell. (c) Recovered phase image of the K562 cell. (d) Phase image of the K562 cell after interpolation.

References

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